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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,998	09/12/2003	David J. Ecker	DIBIS-0002US.P5	7721
58057	7590	12/11/2007	EXAMINER	
Casimir Jones, S.C.			CHUNDURU, SURYAPRABHA	
440 Science Drive			ART UNIT	
SUITE 203			PAPER NUMBER	
Madison, WI 53711			1637	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/660,998

Applicant(s)

ECKER ET AL.

Examiner

Suryaprabha Chunduru

Art Unit

1637

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 46-96 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 46-91 and 95 is/are rejected.
- 7) ☒ Claim(s) 92-94 and 96 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 May 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 15, 2007 has been entered.

***Status of the Application***

2. The action is in response to the RCE filed on November 15, 2007. Currently claims 46-96 are pending. Claims 1-45 are cancelled. New claims 91-96 are added. All arguments and amendment have been fully considered and thoroughly reviewed and deemed persuasive in-part for the reasons that follow. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 84-85, 87-90, 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tatuch et al. (Am. J. Hum. Genet., Vol. 50, pp. 852-858, 1992) in view of Aaserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996).

Tatuch et al. teach a method of claim 84, of characterizing heteroplasmy of a segment of mitochondrial DNA (mtDNA) of a subject comprising (a) providing a sample (see page 853, col. 2, paragraph 1 under methods section);

(b) amplifying said segment of mtDNA obtained from said sample with a pair of primers to obtain a plurality of amplification products (see page 853, col. 2, paragraph 2 under methods section, page 854, col. 1, line 1-2);

(c) determining molecular masses of said amplification products (see page 854, col. 1, line 2-11);

(d) determining base composition of said plurality of amplification products thereby characterizing said heteroplasmy (see page 854, col. 1, paragraphs 1-2, col. 2, paragraph 3 under results section, page 855, col. 2, paragraph 1, and paragraph under discussion section, page 856, col. 1, paragraph 1, page 857, line 1-12).

With regard to claim 85, Tatuch et al. teach that said heteroplasmy is selected from length heteroplasmy (page 854, paragraph 2 under results section, page 855, Fig. 3, col. 2, paragraph 1).

With regard to claim 87, Tatuch et al. teach comparing said heteroplasmy with the plurality of molecular masses of said segment of mtDNA from a plurality of subjects with one or more mitochondrial diseases (see page 855, Fig. 3, col. 2, paragraph 1).

With regard to claim 88, Tatuch et al. teach that said one or more mitochondrial diseases include Leigh disease, MERFF, pyruvate dehydrogenase deficiency (see page 854, col. 2, paragraph 2 under results section, page 857, line 1-26, page 853, col. 1, paragraph 1 under subjects and methods section, col. 2, line 1-10, paragraph 1).

With regard to claim 90, Tatuch et al. teach that said sample from said subject is a forensic evidence sample (autopsy sample) (see page 853, col. 1, paragraph 1 under subjects and methods section, col. 2, line 1-10, paragraph 1).

However Tatuch et al. did not teach determining molecular masses by mass spectrometry.

Aaserud et al. teach a method for accurate measurement of molecular masses of double-stranded DNA by mass spectrometry (see page 1266, abstract, page 1268, col. 1, paragraph 3), wherein Aaserud et al. teach that the method provides accurate molecular weights of its high-resolution mass spectrum from an electrospray ionization/Fourier transform instruments yielding only the correct ds- and ss- base compositions (see page 1266, abstract).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Tatuch et al. in a manner as taught by Aaserud et al. by incorporating measuring base-composition by mass spectrometry for the purpose of enhancing sensitivity of the method for analyzing sequence variations in said target nucleic acid. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Tatuch et al. with a step determining

molecular mass measurement by using mass spectrometry as taught by Aaserud et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in a sensitive comparison of base composition variations in mtDNA and accurate measurement of base compositions in said target because Aaserud et al. explicitly taught that the mass spectrometry measures accurate molecular masses thereby providing correct base compositions of a target nucleic acid (see abstract on page 1266) and such modification is considered as obvious over cited prior art.

E. Claim 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tatuch et al. (Am. J. Hum. Genet., Vol. 50, pp. 852-858, 1992) in view of Aaserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996) as applied to claims 46, 51-52, 54-65, 70-71, 73-85, 89-90 above, and further in view of Baumer et al. (Am J Hum Genet., Vol. 54, pp. 618-630, 1994).

Tatuch et al. in view of Aaserud et al. teach a method of mtDNA analysis as discussed in the section 3A above.

However neither Tatuch et al. nor Aaserud et al. teach analysis of mtDNA from said subject at different ages of the individual to characterize heteroplasmy indicating rate of naturally occurring mutations.

Baumer et al. teach a method for detecting age-related human mtDNA mutations, wherein the method comprises obtaining mtDNA from plurality of tissues at different ages of an individual to detect mtDNA mutations (see page 618, summary, page 621, col. 2, paragraph 2, Fig 2C).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Tatuch et al. in a view of Aaserud et al. by incorporating association of base composition differences with a mtDNA disease as taught by Baumer et al. for the purpose of detecting naturally occurring mutations.. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Tatuch et al. in view of Aaserud et al. with the teachings of Baumer et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in detecting age related mtDNA mutations in an individual with progressing age because Baumer et al. explicitly taught age related accumulation of mtDNA deletions and the progression of mtDNA diseases with the progression of age (see page 618, summary) and such modification is considered as obvious over cited prior art.

***Response to arguments:***

4. With regard to the rejection of claims 46, 51-52, 54-65, 70-71, 73-85, 89-90 under 35 USC 103(a) as being obvious over Parson et al. in view of Aaserud et al., Applicants' arguments are fully considered and found persuasive in-part. Applicants argue that the combination of Parsons and Aaserud et al. does not teach or suggest comparing base compositions of said one or more amplification products with a database comprising known base compositions from said one or more segments of mtDNA from plurality of subjects and fail to teach relative amounts of said amplification products. Applicants also argue that there is no motivation to combine the references and assert that Parson teaches away from the claimed invention as Parson reference characterizes mtDNA by sequence analysis as opposed to the instant claims reciting determining molecular masses by mass spectrometry, without sequencing.

Applicants' arguments are found unpersuasive. Examiner notes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, specific motivation is provided in the rejection, which states that One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Parson et al. with a step determining molecular mass measurement by using mass spectrometry as taught by Aaserud et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in a sensitive comparison of base composition variations in mtDNA and accurate measurement of base compositions in said target because Aaserud et al. explicitly taught that the mass spectrometry measures accurate molecular masses thereby providing correct base compositions of a target nucleic acid (see abstract on page 1266) and such modification is considered as obvious over cited prior art.

Further as noted in MPEP 2145, "A prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness; however, "the nature of the teaching is highly relevant and must be weighed in substance. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994), a teaching away, is a significant factor to be considered as "teaching in". In the instant context Parson reference teaches determining base composition



using sequencing, however, Aaserud et al. teach the mass spectrometry analysis of base composition without the use of sequencing, which is considered as a teaching in factor.

With regard to the age of the references examiner notes that the mere age of the references is not persuasive of the unobviousness of the combination of their teachings, absent evidence that, notwithstanding knowledge of the references, the art tried and failed to solve the problem.” In re Wright, 569 F.2d 1124, 1127, 193 USPQ 332, 335 (CCPA 1977) (100 year old patent was properly relied upon in a rejection based on a combination of references.). See also Ex parte Meyer, 6 USPQ2d 1966 (Bd. Pat. App. & Inter. 1988) (length of time between the issuance of prior art patents relied upon (1920 and 1976) was not persuasive of unobviousness. In the instant case, it is obvious to one skilled in the art to modify the method of Parson with mass spectrometry analysis to determine the base composition of amplified products accurately without sequencing as discussed in the rejection.

With regard to the AFDIL database as not an equivalent of FBI database for mtDNA, Applicants’ arguments are found unpersuasive, because, AFDIL is the part of FBI of the country in which the study was performed and the reference clearly indicates that the US and British Caucasian databases are used to perform forensic analysis comparison of the mtDNA segments.

With regard to the arguments regarding heteroplasmy determination, Applicants’ arguments are fully considered and found persuasive and the rejection of claims 84 and 85, 89-90 is moot.

With regard to the arguments based on reasonable expectation of success and the analogy to the previous office action, Applicants’ arguments are found unpersuasive. The situation is different in the instant context, Aaserud et al. taught the significance of determining base

composition of PCR amplified products using mass spectrometry and the legal standard for “reasonable expectation of success” is provided by caselaw and is summarized in MPEP 2144.08, which notes “obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , In re O'Farrell , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).” In this factual case, there is express suggestion in the prior art that the Parson teaches determination of base composition using PCR amplification and sequencing it is obvious to modify the method of Parson with the mass spectrometry analysis as taught by Aaserud et al. to accurately determine base composition, without the necessity of sequencing of amplified products. This sufficient for a reasonable expectation of success. Accordingly the rejection is maintained herein for claims 46, 51-52, 54-65, 70-71, 73-83. The limitations of the new claim 91 is within the scope of the rejection. Therefore the new claim 91, which is dependent on rejected claim 46 is herein rejected under the same rejection.

5. With regard to the rejection of claims 53 and 72 under 35 USC 103(a) as being obvious over Parson in view of Aaserud et al. and further in view of Oefner, Applicants argue that since the combination of Parson in view of Aaserud et al. fail to render the independent claims 46 and 65 obvious, Oefner does not remedy the deficiencies of said combination. Applicants' arguments are found unpersuasive. As discussed above, the combination of Parson in view of Aaserud et al. does render the independent claims obvious and it is obvious to modify the teachings of Parson in view of Aaserud et al. further in view of Oefner as discussed in the rejection. Accordingly the rejection of claims 53 and 72 is maintained.

6. With regard to the rejection of claims 87-88 under 35 USC 103(a) as being obvious over Parson in view of Aaserud et al. and further in view of Howard, Applicants' arguments are fully considered and found persuasive and the rejection is withdrawn herein.
7. With regard to the rejection of claims 47-50, 66-69 under 35 USC 103(a) as being obvious over parson in view of Aaserud et al. and further in view of Torroni, Applicants argue that since the combination of Parson in view of Aaserud et al. fail to render the independent claims 46 and 65 obvious, Torroni does not remedy the deficiencies of said combination. Applicants' arguments are found unpersuasive. As discussed above, the combination of Parson in view of Aaserud et al. does render the independent claims obvious and it is obvious to modify the teachings of Parson in view of Aaserud et al. further in view of Torroni as discussed in the rejection. Accordingly the rejection of claims 47-50, 66-69 is maintained.
8. With regard to the rejection of claim 86 under 35 USC 103(a) as being obvious over Parson in view of Aaserud et al. and further in view of Baumer, Applicants' arguments are fully considered and found persuasive and the rejection is withdrawn herein.

***Allowable Subject Matter***

Claims 92-94, and 96 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru  
Primary Examiner  
Art Unit 1637

  
SURYAPRABHA CHUNDURU 12/10/07  
PRIMARY EXAMINER